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TITLE: A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness

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6. AUTHOR(S)
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VA Palo Alto Health Care System/PAVIR
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The primary objective is to investigate yoga for the treatment of chronic pain in veterans with Gulf War Illness (GWI). A secondary objective is to provide veterans with skills in yoga breathing, postures, and meditation that can be used to promote health and well-being. One hundred (100) patients with GWI will be recruited and assigned with equal probability to one of two treatment groups: Yoga Treatment Group or a Pain Support control group. Through this reporting period, a total of twenty-five (n=25) veterans have enrolled into the study; the second study cohort of yoga and pain management (control) classes are currently in progress.

15. SUBJECT TERMS
Chronic Pain, Gulf War Illness, Chronic Illness, Veterans, Chronic Disease, Chronic Pain, Disease Attributes, Nervous System Diseases, Neurologic Manifestations, Pain, Pathologic Processes, Signs and Symptoms.

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Many military personnel who participated in the Gulf War in 1990-1991 reported negative health consequences subsequent to their deployment, the most prevalent involving a triad of symptoms that include fatigue, pain, and cognitive disturbances, commonly referred to as "Gulf War Illness" (GWI). No clear, unifying patho-physiological disease process or effective treatment has yet been identified for GWI. Results from a diverse spectrum of research studies support the view that veterans with GWI are medically ill, but that the physiological abnormalities that contribute to their illness are not currently well understood nor sufficiently treated by conventional medicine. While the cause of GWI remains unknown, a potential link between GWI and autonomic nervous system (ANS) dysregulation has been suggested. Yoga has been suggested to exert its therapeutic effects through adjusting imbalances in the ANS. In addition, yoga has been shown to be clinically effective in treating many of the physical symptoms typically found in GWI including chronic pain and fatigue. As chronic pain is perhaps the most prevalent and debilitating symptom of GWI, we have chosen pain as the primary target of our intervention. To date, no improvements in pain have been reported in any clinical trial involving GWI and no published studies have investigated yoga as an intervention for GWI.

The primary objective is to investigate yoga for the treatment of chronic pain in veterans with GWI and determine if the health-related benefits of yoga persist after the termination of the treatment plan. A secondary objective is to provide veterans with skills in yoga breathing, postures, and meditation that can be used to promote health and well-being. One hundred (100) patients with GWI will be recruited and assigned with equal probability to one of two treatment groups: Yoga Treatment Group or a Pain Support control group. The control group has been carefully designed to control for many features of a yoga intervention. Patients in both groups will attend weekly classes for 10 weeks, followed by six months of follow-up testing. Monitoring will include periodic measures of pain, fatigue, quality of life, and ANS function.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Chronic Pain, Gulf War Illness, Chronic Illness, Veterans, Chronic Disease, Chronic Pain, Disease Attributes, Nervous System Diseases, Neurologic Manifestations, Pain, Pathologic Processes, Signs and Symptoms.

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

The overarching goals include:

1. Develop a manualized yoga treatment protocol for veterans with chronic pain. (100% complete)

2. Develop a manualized behavioral treatment protocol for veterans with chronic pain. (100% complete)

3. Conduct a randomized clinical trial (N=100) to evaluate the efficacy of yoga in reducing chronic pain in Gulf War veterans as compared to a pain support control group. (In progress)

4. Determine if the health-related benefits of treatment persist after termination of the program.

What was accomplished under these goals?

During this reporting period, the goals encompassed four specific objectives. Each of these objectives involved subtasks and milestones, which are described below.

1. Major Task 1: Prepare standard protocols for study.
    a. Subtask 1: Prepare manualized treatments for study.
        i. Milestone: Develop a manualized yoga treatment protocol for Veterans with chronic pain.
            - 100% complete.
        ii. Milestone: Develop a manualized behavioral treatment protocol for Veterans with chronic pain.
            - 100% complete.
2. Major Task 2: Study preparation.
    a. Subtask 1: Obtain regulatory approval.
        i. Milestone: Receive approval from the Stanford IRB, in addition to the Human Research Protection Office (HRPO).
            - 100% complete.
    b. Subtask 2: Identify CBOC to use as a second site.
        i. Milestone: Identify a suitable local CBOC.
            - In progress.
    c. Subtask 3: Recruit and train study staff.
        i. Milestone: Hire study staff.
            - 100% complete for hiring study coordinator and instructors for yoga and behavioral interventions.
            - In progress for hiring an additional behavioral intervention instructor and replacement database manager.
    d. Subtask 4: Facilitate training, supervision, and fidelity checks with new staff.
        i. Milestone: Maintain trained and available study staff throughout the duration of the trial.
            - Ongoing.
    e. Subtask 5: Set up Access database.
        i. Milestone: Create a functioning Access database, complete with fillable forms for data entry.
            - 100% complete.
3. Run randomized controlled study.
    a. Subtask 1: Conduct study and report findings.
        i. Milestone: Consent, screen, and enroll first participant and begin the study.
            - 100% complete. Enrolled the first participant on 06/01/15; began study on 06/16/15.
            - Recruited participants through various media (flyers, mass mailings, targeted recruitment via clinics, Facebook, web-based recruiting, etc.).
            - Screened potential participants using telephone screening waiver of consent (170 local Veterans + 475 Veterans nationwide).
            - Consented, screened, and enrolled participants into the study and commenced the study (25 Veterans).
            - Evaluated and randomly assigned participants to one of the two treatment groups: Yoga and Pain Management Wellness Group.
            - Began study (two cohorts) (n=25).
        ii. Milestone: Collect data from the end of treatment and follow-up assessments.
            - In progress; collected data for the end of treatment (08/18-21/15); first follow-up (week 18 – 10/13/15) for the first cohort.
        iii. Assessed participants at 2, 4, 6, 8, 10 week timeframe.
            a. Collected data for the end of treatment (08/18-21/15) for the first cohort.
            - Complete follow-up assessments at 2, 4, and 6 month timeframe.
4. Data analysis, report findings
    a. Subtask 1: Coordinate with Data Manager for monitoring data collection.
        i. Milestone: Report results from data analyses.
            - Not yet applicable but actively maintaining and monitoring data collection.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

1. Study preparation.
    a. Identify CBOC to use as a second site and recruit Veterans for that site.
        - Continue collaborating with a General Medicine Physician at the San Jose CBOC and possibly the Fremont CBOC, and recruit Veterans for those sites for a cohort to begin in January 2016.
    b. Recruit and train study staff.
        - Train an additional behavioral intervention instructor and replacement database manager.
    c. Facilitated training, supervision, and fidelity checks with new staff.
        - Maintain available study staff throughout the duration of the trial.
2. Run randomized controlled study.
    a. Continue to conduct study and report findings.
        - Continue to recruit participants through various media (flyers, mass mailings, targeted recruitment via clinics, Facebook, web-based recruiting, etc.).
            - Possibility of an advertisement in the *Disabled American Veteran* Magazine.
        - Consent, screen, and enroll participants into the study.
        - Evaluate and randomly assign participants to one of the two treatment groups: Yoga and Pain Management Wellness Group. Begin new cohorts.
        - Assess participants at 2, 4, 6, 8, 10 week timeframe.
            - Cohort B:
                - Week 6: 10/20/15
                - Week 8: 11/03/15
                - Week 10: 11/17/15
        - Collect data for the end of treatment and follow-up assessments at 2, 4, and 6 month timeframe.
            - Cohort A:
                - 2 month: 10/13/15
                - 4 month: 12/08/15
                - 6 month: 02/02/15
            - Cohort B:
                - Week 10: 11/17/15
                - 2 month: 01/12/16
                - 4 month: 03/08/15
                - 6 month: 05/03/15
        - In all phases of the study, retain participants who have consented and enrolled in the study.
            - Remind participants of classes on a weekly basis and of appointments in advance.
            - Keep participants engaged in the classes.
3. Data analysis, report findings.
    a. Maintain monitoring of data collection.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

During this reporting period, a community based outpatient clinic (CBOC) was not identified for use as a second study site as projected; this was due to the fact that VA Palo Alto continued/s to be a viable location for the recruitment of Veterans into the study. We have currently enrolled two cohorts of patients at VA Palo Alto into the study.

Actual or anticipated problems or delays and actions or plans to resolve them

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Study recruitment was/is anticipated to continue to be a challenge in this study. The specific recruitment challenge is that Veterans must have been enlisted in the military during the first Gulf War (1990-1991). During this reporting period, we employed several forms of mass mailings. This recruitment method had relatively low yields.

- In May 2015, the study's information was publicized in a national War Related Illness and Injury Study Center (WRIISC) newsletter.
  - 475 Veterans contacted the study (7 local Veterans); 5 were eligible; 1 consented, screened, and enrolled in the study.
- In June/July 2015, VA SF/UCSF collaborator, Dr. Linda Chao, mailed 241 Gulf War I Veterans in the greater Bay Area; 85 letters (35%) were returned to the sender.
  - 12 Veterans replied; 8 were eligible; 1 consented, screened, and enrolled in the study.
- In July 2015, Markots Marketing sent 11,383 postcards to Veterans between the ages of 45-85.
  - 11 Veterans contacted the study; 2 were eligible; 1 consented, screened, and enrolled in the study.

Going forward, we anticipate that recruitment will continue to be a challenge. To address this challenge, we will continue to employ a combination of multiple recruitment methods to *actively* advertise our study:

- Recruit weekly at VA Palo Alto Farmer's Market and in the lobby of the main hospital building.
- Place study flyers in high-traffic areas of VA Palo Alto on a weekly basis.
- Mail local Veterans from the Gulf War Registry a second time.
- Follow up with Veterans who, for various reasons, were previously unable to join our cohorts.
- Explore the possibility of an advertisement in the *Disabled American Veteran* Magazine.
- Utilize social media, in addition to websites, to broaden our reach and have an online presence.
- Present our study to VA clinicians/medical care teams and providing study flyers for their clinics.
- Collaborating with the Veteran Service Organizations (VSO) and various other veteran groups.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals.

Nothing to report.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.
  Journal publications.

Nothing to report.

Books or other non-periodical, one-time publications

Nothing to report.

Other publications, conference papers, and presentations.

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Peter Bayley, PhD
Project Role:	Project Director
Nearest person month worked:	2
Contribution to Project:	Project management, personnel training, study
Name:	Rachael Cho
Project Role:	Research Assistant/Study Coordinator
Nearest person month worked:	9
Contribution to Project:	Ms. Cho is the Study Coordinator and has performed work in the area of patient screening, personnel management, study advertising, and study regulatory activity.
Name:	Louise Mahoney
Project Role:	Co-Investigator
Nearest person month worked:	2
Contribution to Project:	Developed yoga treatment manual with team of yoga therapists and consultants. Lead patients in the yoga group and managed the group.
Name:	Jessica Schienle
Project Role:	Pain Support Group Leader
Nearest person month worked:	1
Contribution to Project:	Edited and developed the manual for the control condition (Behavioral Pain Intervention). Lead patients in the control group.
Name:	Michael Nolasco
Project Role:	Clinical Research Assistant I
Nearest person month worked:	3
Contribution to Project:	Developing the recruitment database and study database and oversaw data input.
Name:	Serenity Sersecion
Project Role:	Pain Support Group Leader
Nearest person month worked:	1
Contribution to Project:	Developed the treatment in the manual for the control condition (Behavioral Pain Intervention).
Name:	Linda Collery
Project Role:	Yoga Leader
Nearest person month worked:	1
Contribution to Project:	Lead participants in yoga classes. Data input and patient recruitment.
Name:	Danae Moore-Downing
Project Role:	Yoga Leader
Nearest person month worked:	1
Contribution to Project:	Lead participants in yoga classes. Data input and patient recruitment
Name:	Michael Stanton
Project Role:	Postdoctoral Research Fellow/Pain Support Group Leader
Nearest person month worked:	1
Contribution to Project:	Edited and developed the manual for the control condition (Behavioral Pain Intervention). Lead patients in the control group.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

A previously pending grant is now active:

GRANT 1 I01 RX001485-01 (PI: Bayley)
07/01/2015 – 06/28/2019
2.40 calendar
VA RR&D Merit Review
$1,014,173
Breathing Meditation Intervention for Post-Traumatic Stress Disorder

The major goals of this project are to investigate the efficacy of breathing meditation for treating symptoms of PTSD in Veterans and to compare it to the standard of care (cognitive processing therapy).

What other organizations were involved as partners?

- Defense Manpower Data Center (DMDC) Reporting System
  Seaside, CA
  Collaboration to assist with patient recruitment. DMDC is a branch of the Department of Defense and maintains data, such as names, address, and phone numbers, on Gulf War Veterans.
- Linda Chao, PhD (VA San Francisco Medical Center/UCSF)
  San Francisco, California
  Collaboration to assist with patient recruitment. Dr. Chao mailed our study recruitment letters, flyers, and response cards to her past Gulf War subjects from VA San Francisco who have consented to being contacted for future research studies.

8. SPECIAL REPORTING REQUIREMENTS:n/a

9. APPENDICES: n/a